

PATENT COOPERATION TREATY

Translation

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing
(day/month/year)

Applicant's or agent's file reference
2002-017

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/EP2004/005268

International filing date (day/month/year)

17.05.2004

Priority date (day/month/year)

19.05.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant

EBEWE PHARMA GES.M.B.H. NFG.KG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/005268

Box No. 1

Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language
_____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
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International application No.

PCT/EP2004/005268

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-10</u>	YES
	Claims _____	NO
Inventive step (IS)	Claims _____	YES
	Claims <u>1-10</u>	NO
Industrial applicability (IA)	Claims <u>1-10</u>	YES
	Claims _____	NO

2. Citations and explanations:

1 Reference is made in the present report to the following documents:

D1: WO 00/23070 A1 (BEN VENUE LABORATORIES, INC; ANEVSKI, PHILLIP, J) 27 April 2000 (2000-04-27)

D2: WO 99/33780 A1 (SCHEIN PHARMACEUTICAL, INC) 8 July 1999 (1999-07-08)

D3: EP 0 645 145 A (BRISTOL-MYERS SQUIBB COMPANY; SQUIBB BRISTOL MYERS CO) 29 March 1995 (1995-03-29)

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the requirements of PCT Article 33(1) because the subject matter of claim 1 does not involve an inventive step within the meaning of PCT Article 33(3).

Document D1 discloses (the references in brackets relate to this document) a process for purifying non-ionic surface-active substances. Polysorbat 80 and Cremophor in a solvent solution are purified with activated carbon and Amberlite ion exchange resin. The solubiliser is removed free of pyrogen to

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Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

give the pure Cremophor. Paclitaxel is dissolved in the purified Cremophor and anhydrous ethanol. The solution is filtered and dispensed into ampoules, which are sealed and tested for stability. The Paclitaxel solution with purified Cremophor is found to be more stable. In place of the Cremophor it is also possible to employ Polysorbat 80 purified in the same way. (Page 2, line 14 - page 3, line 27; page 6, line 7 - page 7, line 28; table 3; page 14, line 3 - page 16, line 9; claims 1, 7-9, 13, 14, 18.)

The subject matter of claim 1 therefore differs from the process disclosed in D1 solely in that, at the time of cationic exchange, the active substance is already present in the solution with Chremophor. As in D1, a stable preparation is obtained.

The problem on which the application is based is therefore an alternative method for the production of a stable injectable formulation comprising an antineoplastic substance, a solvent and, optionally, a solubilization agent.

The solution consists in treating a formulation comprising an antineoplastic active substance, a solvent and a solubilization agent with a cation exchanger.

This solution cannot be regarded as being inventive, since the sole difference from the prior art is that the active substance is already present in the formulation with solvent and solubilization agent when treated with the cationic exchanger: in D1 (example 1) the Cremophor EL, in solution in